

**b.) Amendments to the Claims:**

The following is a list of all claims that are pending in the application as of this office action, presented irrespective of whether the claim(s) remains under examination in the application. Status identifiers precede each claim.

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1. (Withdrawn)

2. (Withdrawn)

3. (Withdrawn)

4. (Withdrawn)

5. (Withdrawn)

6. (Withdrawn)

7. (Withdrawn)

8. (Withdrawn)

9. (Withdrawn)

10. (Withdrawn)

11. (Withdrawn).

12. (Amended) An enzyme having significant (as herein defined) sequence similarity to DAOCS, wherein the side chain binding site of penicillin N ~~or~~ DAOCS is modified ~~and~~ at at least one of the following sites wherein at least one amino acid residue is changed to

another amino acid residue or is deleted: Thr72, Arg74, Arg75, Glu156, Leu158, Arg160, Arg162, Leu186, Ser187, Phe225, Phe264, Arg266, Asp301, Tyr302, Val303, Asn304; and/or at least one additional amino acid residue is inserted within the region 300-311; provided that other residues interacting with the above may be changed in order to accommodate the change in one of the above;

wherein the modifications:

permit the enzyme to accept unnatural substrates; and/or

enable the enzyme to produce unnatural products; and/or

enhance the ability of the enzyme to produce useful products.

13. (Amended) An enzyme having significant (as herein defined) sequence similarity to DAOCS, wherein the penicillin/cephalosporin binding site of penicillin N ~~or DAOC~~ is modified ~~and~~ at at least one of the following amino acid residues ~~is changed or deleted~~: Ile 88, Arg160, Arg162, Phe164, Met180, Thr190, Ile192, Phe225, Pro241, Val245, Val262, Phe264, Ile305, Arg 306, and Arg 307 wherein said at least one of the amino acid residues is changed or deleted; and/or at least one additional amino acid residue is inserted within the region 300-311; provided that other residues interacting with the above may be changed in order to accommodate the change in one of the above;

wherein the modifications:

permit the enzyme to accept unnatural substrates; and/or

enable the enzyme to produce unnatural products; and/or

enhance the ability of the enzyme to produce useful products.

14. (Amended) An enzyme according to claim 12 or 13 which is a mutant of DAOCS ~~or DACS or DAOC/DACS~~.

15. (Withdrawn)

16. (Withdrawn)

17. (Withdrawn)

18. (Withdrawn)

19. (Withdrawn)

a: 20. (Withdrawn)

21. (Withdrawn)

22. (Withdrawn)

23. (Withdrawn)

24. (Withdrawn)

25. (Withdrawn)

26. (Withdrawn)

27. (New) The enzyme of claim 12, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

28. (New) The enzyme of claim 13, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

29. (New) The enzyme of claim 14, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

30. (New) An enzyme having significant sequence similarity to DAOCS, wherein the side chain binding site of penicillin N is modified and at least one amino acid residue at one or more of the sites selected from the group consisting of Thr72, Arg74, Arg75, Glu156, Leu158, Arg160, Arg162, Leu186, Ser187, Phe225, Phe264, Arg266, Asp301, Tyr302, Val303, and Asn304 is changed to another amino acid residue or is deleted.

31. (New) The enzyme of claim 30 wherein the penicillin/cephalosporin binding site of penicillin N is modified and wherein at least one of the amino acid residues selected from the group consisting of Ile88, Arg160, Arg162, Phe164, Met180, Thr190, Ile192, Phe225, Pro241, Val245, Val262, Phe264, Ile305, Arg 306, and Arg307 is changed or deleted.

32. (New) The enzyme of claim 30, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

33. (New) An enzyme having significant sequence similarity to DAOCS, wherein the side chain binding site of penicillin N is modified and at least one additional amino acid residue is inserted within the region 300-311.

34. (New) The enzyme of claim 33 wherein the penicillin/cephalosporin binding site of penicillin N is modified and wherein at least one of the amino acid residues selected from the group consisting of Ile88, Arg160, Arg162, Phe164, Met180, Thr190, Ile192, Phe225, Pro241, Val245, Val262, Phe264, Ile305, Arg 306, and Arg307 is changed or deleted.

35. (New) The enzyme of claim 33, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

36. (New) An enzyme having significant sequence similarity to DAOCS, wherein the penicillin/cephalosporin binding site of penicillin N is modified at one or more of the amino acid residues selected from the group consisting of Ile88, Arg160, Arg162, Phe164, Met180, Thr190, Ile192, Phe225, Pro241, Val245, Val262, Phe264, Ile305, Arg306, and Arg307 is changed or deleted.
37. (New) The enzyme of claim 36, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.
38. (New) An enzyme having significant sequence similarity to DAOCS, wherein the penicillin/cephalosporin binding site of penicillin N is modified and at least one additional amino acid residue is inserted within the region 300-311.
39. (New) The enzyme of claim 38, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.
40. (New) The enzyme of claim 38 wherein the penicillin/cephalosporin binding site of penicillin N is modified and wherein at least one of the amino acid residues selected from the group consisting of Ile88, Arg160, Arg162, Phe164, Met180, Thr190, Ile192, Phe225, Pro241, Val245, Val262, Phe264, Ile305, Arg306, and Arg307 is changed or deleted.
41. (New) An enzyme having a significant sequence similarity to DAOCS wherein the penicillin binding site is modified wherein at least one of the following amino acid residues is changed or deleted; Thr72, Arg74, Arg75, Glu156, Leu158, Arg160, Arg162, Leu186, Ser187, Phe225, Phe264, Arg266, Asp301, Tyr302, Val303, Asn304, Ile88, Phe164, Met180, Thr190, Ile192, Pro241, Val245, Val262, Ile305, Arg306, and Arg307.
42. (New) A method of producing beta-lactams of the penicillin or cephalosporin families using an enzyme having significant sequence similarity to DAOCS, wherein the side chain binding site of penicillin N is modified at at least one of the following sites

deleted: Thr72, Arg74, Arg75, Glu156, Leu158, Arg160, Arg162, Leu186, Ser187, Phe225, Phe264, Arg266, Asp301, Tyr302, Val303, Asn304; and/or at least one additional amino acid residue is inserted within the region 300-311; provided that other residues interacting with the above may be changed in order to accommodate the change in one of the above.

43. (New) A method of producing beta-lactams of the penicillin or cephalosporin families using an enzyme having significant sequence similarity to DAOCS, wherein the penicillin/cephalosporin binding site of penicillin N is modified at at least one of the following amino acid residues: Ile88, Arg160, Arg162, Phe164, Met180, Thr190, Ile192, Phe225, Pro241, Val245, Val262, Phe264, Ile305, Arg306, and Arg307 wherein said at least one of the amino acid residues is changed or deleted; and/or at least one additional amino acid residue is inserted within the region 300-311; provided that other residues interacting with the above may be changed in order to accommodate the change in one of the above.

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